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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/740,242	12/18/2000	James Varani	1718-012	4901

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/740,242	VARANI ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment, response to restriction and remarks dated 6-19-06 is acknowledged.

Claims 1-15 are pending in the instant application.

RESPONSE TO RESTRICTION/ELECTION

1. Applicants' election with traverse of group II, in the reply filed on 6-19-06 is acknowledged. The traversal is on the grounds that claim 15 now requires treating collagen degradation caused by acne, not acne per se and therefore group III is not distinct from group II. Examiner agrees that in view of the amendment to claim 15, that there is no distinction between groups II and I. Accordingly claims 8-15 have been considered for examination. With respect to group I, it is argued that with the present amendment all of the claims now require that the composition preferentially inhibit MMP-1/8/13 with respect to MMP-9/2, or that the method achieve the same inhibitory effect. It is argued that the use of the claimed composition for treating different methods to the extent the claims recite is not the practice of an artisan or ordinary skill in the art. Therefore, it is argued that the claims of group I be combined with group (now claims 8-15). Applicants' arguments are not persuasive because the claims 1, 3, 6 & 7 of group I are directed to a composition comprising "a compound", without even specifying any specific amounts. Applicants have not provided any evidence of record that any compound inhibits MMP 1/8/13, with respect to MMP-9 at any concentrations. Accordingly, instant claims encompass any compound, which depending on the

amounts chosen in the composition does not necessarily possess the claimed functional characteristics whereas the method claims of group II does require the compounds in amounts so as to achieve the claimed function. For the above reasons, the restriction requirement between group I and group II is still deemed to be proper and accordingly, the rejection has been made Final.

DOUBLE PATENTING REJECTION

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 8-15 are rejected on the grounds of nonstatutory obviousness type double patenting as being unpatentable over claims 1-13 of US Patent No. 6,130,254; claims 1-23 of US Patent No. 6,683,069; claims 1-38 of US 6,630,516 claims 1-18 of US Patent 6,919,072 and claims 1-12 of US Patent 7,141,238. Although the conflicting

claims are not identical, they are not patentably distinct from each other because of the following reasons: all of the above sets of patented claims recite a method of either inhibiting or delaying the onset of collagen degradation or increasing the procollagen production by the application of an MMP inhibitor (US '254, US '516 and US '072) alone or in combination with other MMP inhibitors or UVA or UVB blockers. Further, the patented claims employ retinoic acid, and other antioxidants such as genistein, green tea etc., and thus meet the instant claimed compounds. With respect to the instant limitations of inhibiting at least one of MMP-1/8/13 with respect to MMP-9, while the above patented claims do not recite the specificity of the inhibitory effect, a careful review of the MMP inhibiting activity of the compounds in the above patents reveal that of inhibitory effect o the claimed compounds is specific to MMP-1 with respect to MMP-9. In particular, see the figure 13 of US '254, col. 5, L 50-55 of US 072 and figure 14 and col. 8 of L 31-47 of US '516, where the effect of the collagen protective (or the MMP inhibitory effect) compounds is more pronounced with respect to MMP-1 as opposed to MMP-9, which clearly meets the instant claimed requirement. While instant claims recite retinoid and UV A and UV B blocking compound in addition to the compounds with the claimed selectivity, which are not present in the above patented claimed. However, the above patents claim compounds with MMP inhibitory activity, which is shown as selective inhibition (from the figures of the patents) and therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ compounds that possess MMP inhibitory activity to reduce collagen degradation, improve collagen biosynthesis etc., in UV damaged or aged skin or

conditions where collagen damaged needs to be restored or improved such as acne affected skin, with an expectation to achieve selective inhibition of the MMPs that cause the degradation of collagen and thus provide a treatment for damaged or aged skin.

3. Claims 6-15 are directed to an invention not patentably distinct from claims1-13 of US Patent No. 6,130,254; claims 1-23 of US Patent No. 6,683,069; claims 1-38 of US 6,630,516 claims 1-18 of US Patent 6,919,072 and claims 1-12 of US Patent 7,141,238, all of which are commonly assigned US Patents.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned patents, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim Rejection 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Clams 8-15 are rejected under35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain the subject matter, which was not described in such a way as o reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant claims are directed a method of improving collagen and fibroblast proliferation in a chronologically aged skin or a method of reducing collagen degradation and improving collagen biosynthesis inhibited in human skin due to exposure of said skin to UV radiation or a method of treating collagen degradation in acne-affected skin, comprising topically applying a compound selective for the inhibition of at least one of MMP-1, MMP-8 and MMP-13 with respect to MMp-9 and optionally MMP-2. Thus, instant claimed methods require administration of a compound with a selective activity (inhibitory) against MMP-1/8/13 with respect to MMP-9. A review of the instant specification reveals that while applicants have provided a rationale for selective inhibition of certain MMPs with respect to others, the specification does not describe what are the compounds that possess the said or claimed properties. On page 11 of the specification, applicants refer to the works of Whittaker et al and the like to determine

which MMPs a given inhibitor selectively inhibits. Applicants also state that the aforementioned article, however, refers to over a hundred MMP inhibitors but only compounds 28, 52, 53 have the claimed selective MMP inhibitory activity. According to the description it appears that not all of the above compounds are equally efficient in inhibiting MMP 1, 8 and 13 with respect to MMP-9. Further, instant specification does not provide any information or description of the compounds (chemical or biological) or their structure-function relationship with respect o the claimed inhibitory activity. While applicants refer to and suggest following the teachings of Whittaker references for the compounds 28, 52 and 53, applicants do not provide evidence as to the testing of any of these compounds in practicing the claimed invention. The entire disclosure devoted to the detailed description of the instant invention deals with testing the collagen production, collagen degradation by the metalloproteinases in photodamaged skin of volunteers or in vitro conditions or in vitro relationship between collagenses to the amount of collagen contraction achieved. Nowhere in the instant specification did applicants provide any evidence of their possession of actual compounds that inhibit MMPs specifically as claimed, and further in achieving the claimed methods. Thus, instant description does not allow one of an ordinary skill in the art to recognize that applicants invented instant claimed invention. Therefore, instant claims fail to comply with the written description requirement.

5. Claims 8-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant invention is directed a method of improving collagen and fibroblast proliferation in a chronologically aged skin or a method of reducing collagen degradation and improving collagen biosynthesis inhibited in human skin due to exposure of said skin to UV radiation or a method of treating collagen degradation in acne-affected skin, comprising topically applying a compound selective for the inhibition of at least one of MMP-1, MMP-8 and MMP-13 with respect to MMp-9 and optionally MMP-2. Thus, instant claimed methods require administration of a compound with a selective activity (inhibitory) against MMP-1/8/13 with respect to MMP-9. Instant invention claims numerous possible compounds (biological as well as chemical) and their derivatives as suitable for claimed selective MMP inhibitory effect.

The state of the art recognizes the importance of collagen degradation in physiological process such as chronological aging, UV or photo damaged skin or acne affected skin. Prior art also recognizes that the loss of collagen or collagen degradation as a result of MMP (enzyme activity) and the different types of MMPs that affect different types of collagen; and inhibition of MMPs in general, by a number of compounds (cytokines, chemical compounds etc.). Furthermore, it is recognized (Whittaker et al articles referenced in the instant specification), that certain compounds have inhibitory activity against different MMPs. The prior art further recognizes treating

photodamaged, UV damaged skin or acne-affected skin by a variety of compounds, some of which might possess MMP inhibiting activity. For example, applicants related US patents such as 6,130,254, 66311516 etc., describe the various ways of treating collagen degradation in chronologically aged or sun-damaged skin. Based on the teachings from the prior art, one of an ordinary skill in the art would readily be able to provide treat a skin due to UV damage or chronological aging by known treatments such as retinol or UV A or UV B inhibiting compounds, during the process of which it is conceivable that the collagen restoration or improvement in the underlying matrix of skin could be achieved.

However, instant claims require a selective inhibition of MMPs in order to reduce collagen degradation or improve procollagen degradation by topically administering a compound with such selective inhibition. However, other than referring to three specific compounds (compounds 28, 50, and 53), applicants do not provide any description as to what compounds are capable of achieving such as effect. Even among the 3 compounds, applicants fail to provide any structural description of the compounds (see the written description rejection above) or their amounts or dosage forms administered to various age groups- because chronological aging is different from UV or photo damaged. Applicants failed to provide any evidence if the above compounds actually increase collagen and fibroblast proliferation (required by independent claim 8), how to prepare the claimed topical formulations containing the above compounds. Applicants fail provide if any other compounds (biological or chemical) are capable of the claimed selective inhibition and thus the claimed improved procollagen biosynthesis and

reduced collagen degradation. In the absence of any description or guidance by the applicants, one of an ordinary skill in the art would not be able make the compounds that possess such activity (other than the three compounds) nor would be able to use the compounds successfully for the claimed invention. This is particularly true because of the fact that even the mentioned (not described) compounds differ in their selective inhibition of various MMPs and applicants have described as to what level of inhibition of MMP 1,8 13 is required with respect to MMP-9 so as to achieve procollagen biosynthesis and reduced collagen degradation. Absent such clear guidance with respect to the types of compounds, structure, their synthesis, dosage forms etc., one of an ordinary skill in the art would have to turn to undue experimentation in order to practice the instant invention. A skilled artisan would have to undertake laborious identification and testing of each of the compounds that might possess such as selective MMP inhibition and further painstakingly test the compounds for their ability to improve collagen or reduce collagen degradation as well as procollagen biosynthesis in the claimed groups of patients.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,837,224, US 6,130,254, US Patent No. 6,683,069; US 6,630,516, US 6,919,072 and US Patent 7,141,238.

The applied references have common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Each of the above patents describe method of reducing collagen degradation, improving collagen in human aged skin and photodamaged skin by administering compounds such as retinoid, glucocorticoid, vitamin D3 etc (explanation under Double Patenting rejection section for the teachings of the patents). The above patents such a

selective inhibition of MMPs (MMP 1 with respect to MMP 9) with the above compounds (see figures showing inhibition of MMPs with retinoid and other compounds in the above patents). Instant claims differ from the above patents in that instant claims require retinoid and UVA or UVB blockers, in addition to the "compounds" which exhibit selective effect, whereas the patents teach inhibition mainly with retinoid compounds. However, each of the above patents clearly describe the biochemistry of various MMPs, involvement of several transcription factors such as AP-1, c-jun, NF-kappa B, claimed EGF-R protein tyrosine kinase etc. in the upregulation or downregulation of various MMPs, compounds that inhibit the said transcription factors 7 kinases, and their role in collagen degradation. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ any of the compounds (in addition to retinoids, UVA or UVB blockers) that inhibit MMPs taught by the above patents alone or in combination with retinoid and UVA/B blockers to inhibit MMPs and thus reduce collagen degradation or improve collagen synthesis because the above patents teach several compounds that inhibit different MMPs at different levels and via different pathways. Accordingly, a skilled artisan would have expected to improve collagen synthesis or reduce collagen degradation in treating various skin conditions such as photo damaged skin, aged skin or in acne affected skin.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -6.30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Examiner
Art Unit 1615

December 9, 2006

LAKSHMI S. CHANNAVAJJALA
PRIMARY EXAMINER